Meetings

Transmutation and Decay of Incorporated Radioisotopes

The physical and chemical factors of radioisotope decay (transmutation, recoil energy, disintegration radiation) play an important role in producing injury when isotopes such as H^3, C^{14}, and P^{32} are incorporated into vital cellular macromolecules. In order to consider such biological effects of transmutation and decay of incorporated isotopes, a meeting was convened at the Vienna headquarters of the International Atomic Energy Agency, 9–13 October 1967. Past and current studies on mutation production, chromosome aberration, macromolecular lesions, and cell survival were reviewed and analyzed to integrate data, concepts, and experimental approaches while identifying new and productive lines of investigations. During the latter part of the meeting, workshop sessions and round-table discussions were held on the biological effects, mechanisms of action, health physics, exploitation of decay effect, and future research directions.

L. E. Feinendegen (Federal Republic of Germany) reviewed the problems associated with the use of labeled molecules in biology and medicine. He considered the nature of the labeled molecule (specificity of labeling, radiochemical purity, kinetic isotope effects), biological factors (precursor incorporation, pool size and equilibrium, isotope dilution by cellular proliferation, cell cycle and radiosensitivity effects, precursor availability (and reutilization) and relative toxicity due to radiation and transmutation of incorporated tritium and C^{14}-, P^{32}-, and S^{35}-labeled substrates.

Subsequently, S. Person (United States) reported on the lethality and mutagenesis in bacteria and phage from incorporated H^3. Lethality was attributed to self-irradiation from the H^3 beta particles. The different killing efficiencies obtained with various H^3 precursors could be explained on the basis of the cellular distribution of decays. Mutagenesis was attributed to molecular rearrangement of H^3-cytosine in DNA following transmutation; 5-H^3-cytosine in DNA was more mutagenic than 6-H^3-cytosine or H^3TdR. A. L. Koch (United States) gave calculations of expected survival curves for H^3 suicide experiments for various models of bacterial growth cycles and experimental results corresponding to a model in which DNA replication proceeded through the cycle. S. Apelgot (France) reviewed H^3, C^{14}, and P^{32} suicide in bacteria; she concluded that the killing of cells from H^3 decay was due exclusively to irradiation by the beta particle, whereas killing from C^{14} and P^{32} decay was due to transmutation. Some of the P^{33} results are similar to those obtained with x-rays (effects of temperature, radical capture, and oxygen), while others are similar to those of ultraviolet irradiations (effect of growth conditions). Comparative tests made with P^{35} indicate that recoil energy of transmutation is not the basis for the lethal effect observed. E. Moustacchi (France) described results on cell killing, mutation, and recombination by P^{32} decays in yeast. The spectrum of mutations induced by P^{32} was similar to that induced by x-rays. However, P^{32} also produced mutations to radioresistance and to abnormal meiosis. The lethal effect of H^3 decays in mammalian cells was reviewed by J. E. Cleaver (United States). Although lethality was due to the H^3 beta particle, there were important differences in survival curves when decays were accumulated in frozen cells (exponential curves) than when decays occurred at 37 degrees (sigmoid curves).

Mutagenesis in drosophila was described by P. Kieft (Netherlands) and by P. Oftedal (Norway). The former reported evidence that could be interpreted as a transmutation effect from H^3 decays; the latter showed that, although P^{32} transmutation caused mutations, the efficiency of mutagenesis was much lower than in bacteria. L. D. Szabo (Hungary) described effects of P^{32} decay causing growth retardation and death in chick embryo; he showed that P^{32} transmutation could produce structural and functional alterations in RNA of isolated ribosomal systems. Repair mechanisms were reviewed by J. Drobnik (C.S.S.R.) who gave evidence from *Escherichia coli* B/r for the rejoining of single-stranded breaks in DNA caused by P^{32} transmutation.

Dosimetric and radiation protection aspects of incorporated radioisotopes were discussed by R. Oliver (United Kingdom). He concluded that the RBE of beta particles from H^3 in DNA or water, relative to x-rays, was between 1 and 1.5; the higher value is obtained at low dose rates. In estimating the dose to DNA from H^3 beta particles it was, however, essential to consider the detailed localization of the H^3 decays. In setting safety limits for radioactive molecules not only the particular isotope but also the chemical nature and biological function of the molecule in which it is incorporated should be taken into account.

A final series of papers dealt with relevant radiochemical considerations. C. D. Adams (United Kingdom) reviewed the redox nature of radiation-induced free radical processes as they relate to both biological and nonbiological material, noting in particular the importance of thermal electrons. In addition, he described the utility of pulse radiolysis and rapid mixing techniques for studying such important radiobiological problems as the relation between free radical radiation chemistry, SH compound protection and oxygen effect, mechanisms of radiosensitizers and the significance of electron migration in the reactivity of sulfur-containing enzymes to radiation. V. Kacena (C.S.S.R.) discussed the chemical effects of a beta decay in atomic and molecular systems, stressing the roles that recoil, electronic excitation, and ionization play in determining the behavior of an organic molecule undergoing a nuclear transformation event. N. Getoff (Austria) summarized the current concepts of the reaction mechanisms of amino acid radiolysis as studied by ESR and pulse radiolysis techniques. He considered the action of the primary products of water radiolysis on sulfur-containing, aromatic, and heterocylic amino acids in oxygenated and air-free solutions and the radiation-induced formation of amino acids.

The panel also discussed the exploitation of decay effects with a view to future research and application. In the case of H^3, although it is an invaluable tracer in biochemical and cellular studies, it is unsuitable in studies of transmutation since the localized effect of

emitted beta particles is predominant. This localized effect is of value as a source of internal radiation in studies of mutagenesis, carcinogenesis, chromosome aberrations, and cell kinetics. As a source of radiation, C^{14} is unsuitable because of its long half-life and the low specific activities currently available. In tracer studies these very factors, however, give C^{14} some advantages over H^3. The transmutation of P^{32} leading to single- and double-strand breaks in DNA may be useful in studying the organization and repair of DNA and chromosomes. The influence of localized effects in proteins may be studied with S^{35} transmutation, and the role of protein inactivation in lethality and mutagenesis assessed. Finally, it was agreed that consideration should be given to possible biological applications of transmutation by neutron activation and the Auger effect.

With respect to protection recommendations, the members concluded that presently there is no justification to modify the recommendations on body burdens on the basis of the contributions of effects resulting from transmutation.

The panel proceedings, including papers, discussions, and workshop summaries, will be published by the International Atomic Energy Agency.

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Calendar of Events

National Meetings

March

4–6. Society of **Toxicology**, Washington, D.C. (C. S. Weil, Mellon Inst., 4400 Fifth Ave., Pittsburgh, Pa. 15213)

4–6. **Technology for Manned Planetary Missions**, New Orleans, La. (Meetings Manager, 1290 Sixth Ave., New York)

4–7. **Neutron Cross Section and Technology** Conf., Washington, D.C. (D. T. Goldman, Natl. Bureau of Standards, Washington, D.C. 20234)

4–8. **Analytical Chemistry and Applied Spectroscopy**, Cleveland, Pa. (R. T. Oliver, Alcoa Research Labs., New Kensington, Pa.)

4–8. **Diagnosis and Treatment of Cardiovascular and Pulmonary Diseases**, Miami Beach, Fla. (H. L. Kruse, Executive